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10/073,293	02/13/2002	Ekaterina Alexsandrovna Tabolina	US-145O	3493

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/073,293	TABOLINA ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-30,32 and 33* is/are pending in the application.

4a) Of the above claim(s) *4-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,32,33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/16/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and remarks, filed 9/12/2007, are acknowledged. Claim 1 is amended. Claims 1, 3-30, and 32-33 are pending. Claims 4-30 are withdrawn. Claims 1, 3, 32 and 33 are currently under examination.

Information Disclosure Statement

The Information Disclosure Statement, filed 11/16/2007, has been considered. An initialed copy is enclosed.

Claim Rejections Withdrawn

The rejection of claim 1, under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "increasing the activity of a protein," is withdrawn in light of applicant's amendment thereto.

The rejection of claim 1, under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "wherein the expression of said protein is increased by transforming said bacterium with the gene coding for said protein," is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 3, 32, and 33 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained for the reasons set forth in the previous office action.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant argues:

1. That the claims have been amended to clarify that between 1 and 5 changes, whether they are deletions, substitutions, insertions, or additions, can possibly occur in the specified sequences.

2. That the variation is very small and well within the skilled artisan's expertise to determine variant proteins which will maintain the required function. Applicant asserts that, at the time of invention, there was a great deal of art concerning amino acid variations and how such changed can effect the three-dimensional structure of a protein. Applicant asserts that, because the skilled artisan could easily and readily predict which changes might be made while still maintaining a functional protein, the genus encompassed by the claims is fully described.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, as set forth in the rejection under U.S.C. 112, second paragraph, below, it is not clear how many amino acids can be changed in the sequence. The claim states that the sequence has "deletions, substitutions, insertions, or additions which total between 1 and 5 amino acids." This could mean that there is an insertion of 1 to 5 amino acids in one place and that there is another insertion of 1 to 5 amino acids in another part of the sequence. Each of these insertions totals between 1 and 5 amino acids.

Regarding argument 2, the variation is not as small as applicant asserts. Even if the total number of amino acids that could be changed in a given sequence was between 1 and 5, the claims are not drawn simply to a sequence. The claims are drawn to a bacterium that contains variants of two proteins (SEQ ID NO:4 and 6). Moreover, if the change was limited to a substitution of a single amino acid in each of these proteins, there would be 9,811,500 possible bacteria. The number encompassed by increasing the number from 1 to 5, and including deletions, insertions, and additions is practically incalculable. Applicant asserts that there is a great deal of art concerning how amino acid variations affect the three-dimensional structure of proteins. This is correct, and the general thrust of this art is that these effects are unpredictable

and that a single change can drastically alter the function of the protein (see, for example, Haynes *et al.*, Electrophoresis, 19:1862-1871, 1998; Skolnick *et al.*, Trends in Biotech., 18:34-39, 2000; Voet *et al.*, Biochemistry, 2nd ed., John Wiley and Sons, Inc, 1995; McGuinness *et al.*, Lancet 337: 514-517, March 1991, all previously cited). Moreover, the function of both proteins listed in the claims is to impart increased resistance to L-amino acids and/or analogs thereof. The way in which these proteins operate is completely unknown. Thus, while the skilled artisan generally knows the effect of said proteins, the actual function of these proteins is unknown; therefore, one could not "easily predict" which changes could be made while maintaining the desired function. Furthermore, the written description requirements are not that one of skill in the art could make or isolate the claimed invention, but that applicant was in possession of the invention at the time of invention. Applicant clearly did not have possession of the enormous genus encompassed by the claims and one of skill in the art would not be able to immediately envisage the members of the genus, as there is substantial variation among the members of the genus, there is not a representative number of species disclosed, and there is no disclosed correlation between the structure and function of the members of the genus.

As outlined previously, the instant claims are drawn to bacteria where the expression of protein A or B and the expression of protein C or D is increased. Proteins A and C comprise the sequences of SEQ ID NO:4 and 6, respectively, while proteins B and D have "deletions, substitutions, insertions, or additions which total between 1 and 5 amino acids, and wherein said protein imparts to the bacterium enhanced resistance to L-amino acids." Any combination of A or C and B or D is encompassed by the claims. Additional dependent claims are drawn to the bacterium where proteins B and D are encoded by the polynucleotide which hybridizes with the sequence complementary to the nucleotide sequence of SEQ ID NO:3 (for protein B) and SEQ ID NO:5 (for protein D), under conditions comprising washing in 1x SSC and 0.1% SDS at 60°C.

The specification discloses proteins with the sequence of SEQ ID NO:4 and 6, which meet the written description provision of 35 USC 112, first paragraph. However, the aforementioned claims encompass a phenomenally large genus of proteins, which combined, encompass an even larger genus of bacteria. As the activity of both proteins is unknown,

applicant has not demonstrated any link between the structure and the function of the claimed proteins.

The specification provides no guidance regarding which of these variants is capable of the required function. Therefore, the specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that

"applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:4 and 6, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides that correlates to the claimed function, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid and/or protein itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

Therefore, only the bacterium with increased expression of SEQ ID NO:4 and SEQ ID NO:6, but not the full breadth of the claims, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115).

The rejection of claims 1, 3, 32, and 33 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated L-amino acid production bacteria belonging to the genus *Escherichia*, wherein the bacterium has increased expression of a protein comprising the amino acid sequence of SEQ ID NO:4 and which has increased expression of a protein comprising the amino acid sequence of SEQ ID NO:6, does not reasonably provide enablement for the claims as drawn, is maintained for the reasons set forth in the previous office action.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues:

1. That the claims have been amended to clarify that between 1 and 5 changes, whether they are deletions, substitutions, insertions, or additions, can possibly occur in the specified sequences.

2. That one of ordinary skill in the art would be able to make and use the bacteria having the proteins with some experimentation, but that such experimentation is merely routine and not undue. Applicant asserts that because so much is known about protein structure and function and because the variation is so small, the variants could be "readily ascertained to be sufficient to maintain function or not."

3. That the examiner's arguments with regard to the number of variants possible for claim 33 does not apply because it is dependent upon claim 1 and further limits it.

4. That the skilled artisan "would not have to make every variant to determine activity, but would be able to use their skill and knowledge that conservative changes increase the chance for retention of activity, whereas non-conservative changes do not.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, as set forth in the rejection under U.S.C. 112, second paragraph, below, it is not clear how many amino acids can be changed in the sequence. The claim states that the sequence has "deletions, substitutions, insertions, or additions which total between 1 and 5 amino acids." This could mean that there is an insertion of 1 to 5 amino acids in one place and that there is another insertion of 1 to 5 amino acids in another part of the sequence. Each of these insertions totals between 1 and 5 amino acids.

Regarding argument 2, the variation is not as small as applicant asserts. Even if the total number of amino acids that could be changed in a given sequence was between 1 and 5, the claims are not drawn simply to a sequence. The claims are drawn to a bacterium that contains variants of two proteins (SEQ ID NO:4 and 6). If the change was limited to a substitution of a single amino acid in each of these proteins, there would be 9,811,500 possible bacteria. The number encompassed by increasing the number from 1 to 5, and including deletions, insertions, and additions is practically incalculable. Applicant asserts that there is a great deal of art concerning how amino acid variations affect the three-dimensional structure of proteins. This is correct, and the general thrust of this art is that these effects are unpredictable and that a single change can drastically alter the function of the protein (see, for example, Haynes *et al.*, Electrophoresis, 19:1862-1871, 1998; Skolnick *et al.*, Trends in Biotech., 18:34-39, 2000; Voet *et al.*, Biochemistry, 2nd ed., John Wiley and Sons, Inc, 1995; McGuinness *et al.*, Lancet 337: 514-517, March 1991, all previously cited). Moreover, the function of both proteins listed in the claims is to impart increased resistance to L-amino acids and/or analogs thereof. The way in which these proteins operate is completely unknown. Thus, while the skilled artisan generally knows the effect of said proteins, the actual function of these proteins is unknown; therefore, one could not "easily predict" which changes could be made while maintaining the desired function. Furthermore, since the activity of these proteins is unknown, one could not test the protein by itself to determine if it imparts increased resistance. One would have to alter the bacterial strain,

then perform growth/resistance tests. Since these proteins impart *increased* resistance, one cannot simply test whether a given strain is resistant or not, but must perform statistical comparisons that require more complex experimentation, including greater numbers of repetitions and more sophisticated analyses. In addition, if a given strain does exhibit increased resistance, further testing would be required to establish that the resistance was a result of increased expression of the altered gene rather than some other mutation in the bacterium.

Regarding argument 3, contrary to applicant's assertion, these arguments do apply. Since the number of changes (each change comprising a total of 1 to 5 altered amino acids) is unlimited, the illustrative numbers used by the examiner are applicable.

Regarding argument 4, the claims are not limited to conservative changes. In fact, the word "conservative" does not appear anywhere in the specification or claims. In molecular biology, the term "conservative" generally refers to substitutions of amino acids with amino acids that have similar properties. This does not apply to insertions, additions, or deletions (which are encompassed by the claims). Even so, as applicant states, "conservative changes increase the chance for retention of activity." This means that, while a conservative change increases the chance for retention of activity, it does not indicate that activity will be retained. The results of such changes are highly unpredictable, and the only way to determine what the results of a given change will be are to make the change and test the resulting bacteria. Therefore, for each given sequence encompassed by the claims, one could only determine if it meets the limitations of the claims by creating and testing the bacteria.

As outlined previously, enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about

the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims are drawn to bacteria where the expression of protein A or B and the expression of protein C or D is increased. Proteins A and C comprise the sequences of SEQ ID NO:4 and 6, respectively, while proteins B and D have "deletions, substitutions, insertions, or additions of 1 to 5 amino acids, and wherein said protein imparts to the bacterium enhanced resistance to L-amino acids." Any combination of A or C and B or D is encompassed by the claims. Additional dependent claims are drawn to the bacterium where proteins B and D are encoded by the polynucleotide which hybridizes with the sequence complementary to the nucleotide sequence of SEQ ID NO:3 (for protein B) and SEQ ID NO:5 (for protein D), under conditions comprising washing in 1x SSC and 0.1% SDS at 60°C.

Breadth of the claims: The claims encompass all bacteria in the genus *Escherichia* that produce any L-amino acids (it is noted that all bacteria produce L-amino acids) wherein said bacteria has increased expression of proteins with an unlimited number of mutations, where each mutation is a deletion, substitution, insertion, or addition of 1 to 5 amino acids, so long as the protein imparts increased resistance to L-amino acids. This includes practically any protein that enhances bacterial resistance to L-amino acids. The claim does not require the bacteria to have enhanced L-amino acid production; however, this is the only disclosed utility of the claimed bacteria.

Guidance of the specification/The existence of working examples: The specification discloses a bacterium that has been transformed by a plasmid bearing the nucleic acid encoding SEQ IDs 4 and 6. The specification further teaches that, under appropriate conditions, said bacterium is capable of producing increased levels of threonine, valine, proline, leucine, and

methionine. The specification lacks any teaching of a protein which comprises an amino acid sequence including deletion, substitution, insertion, or addition of any amino acids in the amino acid sequence of SEQ ID NO: 4 or 6, which has an activity of making bacterium having enhanced resistance to L-amino acids and/or its analogs; or that said proteins would cause enhanced amino acid production. There is no guidance in the specification regarding which amino acids can be deleted, substituted, inserted, or added while retaining activity. The specification further lacks any teaching that a protein comprising either SEQ ID 4 or 6 by itself would lead to enhanced amino acid production, or that the combination would lead to enhanced production of amino acids other than threonine, valine, proline, leucine, and methionine. Besides the amino acid sequences of SEQ IDs 4 and 6, the only information the specification gives on the two proteins is that they are putative transmembrane proteins with unknown function. The specification suggests that they might be membrane proteins with L-amino acid excretion activity (p. 3, lines 11-26), but offers no evidence of this and no information on the regulation of these proteins, and offers no means of determining what the activity of said proteins is.

State of the art: The art is very limited with regard to said proteins. The nucleic acid sequences encoding both SEQ ID 4 and SEQ ID 6 were disclosed in Blattner *et al.* (IDS filed 6/17/2002, document AW) as putative proteins. There is no information in the art regarding the function, or regulation of these proteins. The nucleic acid sequences that comprises regulatory sequences or the proteins that act as promoters or repressors of said proteins are completely unknown. The art does show that mature biologically active forms of many proteins are post-translationally modified by glycosylation, phosphorylation, prenylation, acylation, ubiquitination or one or more of many other modifications and many proteins are only functional if specifically associated or complexed with other molecules including DNA, RNA, proteins and organic and inorganic cofactors. The type of protein modification and the sites modified at a specific cellular state can usually not be determined from the gene sequence alone (Haynes *et al.*, Electrophoresis, 19:1862-1871, 1998, see p. 1863, paragraph bridging cols. 1-2). In addition, Skolnick *et al.* (Trends in Biotech., 18:34-39, 2000) state that sequence-based approaches to function prediction fails to take into account the powerful three-dimensional information displayed by protein structures (p. 34, col. 2, paragraph 4), and that even when the structure is

determined, "knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (p. 35, box 2). The art further shows that the alteration of even a single amino acid can change the activity of a protein. In the case of Sickle-cell anemia, a change of one amino acid from glutamate to valine leads to deformed erythrocytes (Voet *et al.*, Biochemistry, 2nd ed., John Wiley and Sons, Inc, 1995, p. 124). Similarly, in the case of antigen-antibody interaction, McGuinness *et al.* (*Lancet* 337: 514-517, March 1991) taught that a point mutation generating a single amino acid change in a P1.16-specific epitope in the VR2 region of the *porA* gene of a strain of *Neisseria meningitidis* of subtype P1.7,16 resulted in "striking changes in the structural and immunological properties of the class 1 protein" of this isolate (see abstract and page 514). Thus, the alteration of even a single amino acid can lead to substantial changes in a protein, which might or might not enhance the activity of the protein. Claim 1 requires that activity of protein C or D be enhanced. However, there is no means provided in the specification to quantify the activity of said proteins. Without knowing the function of said proteins, one would not know how to assay the activity of said proteins. Moreover, the regulation of protein expression is a complex process that is completely undescribed regarding the putative proteins of the instant invention. There is no description of the structure or activity of the promoter necessary for transcription or whether there is a repressor, inducer, or sigma factor involved. There is no information in the art regarding whether the regulation of these proteins is cis-acting or trans-acting or whether the genes are under positive or negative control.

Therefore, in view of the lack of support in the art and specification, it would require undue experimentation on the part of the skilled artisan to make and use the bacteria as claimed; therefore the full scope of the claims is not enabled.

New Claim Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 32, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the phrase "said sequence has deletions, substitutions, insertions, or additions which total between 1 and 5 amino acids." It is not clear how many amino acids can be changed in the sequence. The claim states that the sequence has "deletions, substitutions, insertions, or additions which total between 1 and 5 amino acids." This could mean that there is an insertion of 1 to 5 amino acids in one place and that there is another insertion of 1 to 5 amino acids in another part of the sequence. Each of these insertions totals between 1 and 5 amino acids. Applicant appears to be arguing, in their remarks, that the total number altered amino acids in the entire sequence is between 1 and 5. If this is the case, it is advised that applicant amend the claim to read, "sequence of SEQ ID NO:4, except that a total of 1 to 5 amino acids are deleted, substituted, inserted, or added."

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brian Gangle
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ROBERT A. ZEMAN
PRIMARY EXAMINER